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# Public Health Reports

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## UNITED STATES.

[Reports to the Supervising Surgeon-General United States Marine-Hospital Service.]

*The bubonic plague bacillus as studied at the Pasteur Institute.*

NO. 5 RUE DE BASSANO, PARIS, April 21, 1897.

SIR: I have the honor to submit for your consideration the following observations upon my studies upon the bubonic plague, with a full consciousness that they embrace nothing new, but with the hope that at this time they will possibly prove of some interest.

The bubonic plague, or pest, is an acute, contagious, communicable disease, primarily, it is now supposed, affecting the lower animals, as rats, mice, hogs, dogs, etc., and by them communicable to man. The specific organism of the disease was first discovered and described by Kitasato and Yersin, working independently and at some distance from each other, and the first published description which appeared in the United States was that of Kitasato, which was extensively quoted, and at this date is somewhat misleading. By him the organism was likened in size and appearance to that of chicken cholera, a small fine bacillus with rounded ends, staining well with the ordinary basic aniline dyes. In reality the organism is a cocco-bacillus, almost as broad as long, about two micromillimeters in greatest diameter, staining readily, it is true, with the ordinary aniline dyes, but also very easily overstaining with them, and its true characters are very apt to be overlooked. The best stain is a 1 per cent solution of thionin, carbolized, colored with which its true characteristics stand revealed, and it is seen to be, as said before, a cocco-bacillus, staining more deeply at the poles than in the center, and forming sometimes chains of three or four elements. It is completely decolorized by the method of Gram, and this is a point which is insisted on with much earnestness by Professor Roux. It grows readily upon ordinary culture media, as peptone-agar, peptone gelatine, and peptone bouillon. Upon agar the separate colonies are very small, round in shape, almost transparent by transmitted, and white by reflected, light. In bouillon, under ordinary conditions of temperature, it forms flakes or flocculi, which rapidly sink to the bottom of the test tube, leaving the liquid above clear. So characteristic is this appearance

that at the Institute Pasteur, in seeking to make pure cultures in bouillon, it has passed into a proverb that if the bouillon is turbid it is useless to examine the growth microscopically, for the culture is not pure. Examined in the hanging drop the microbe is perfectly devoid of automobility.

In old cultures, both on agar and bouillon, the organism rapidly assumes involution forms, some of which are very curious, and most prominent among them is that of a rather long, slender bacillus, segmented and presenting a vacuolated appearance. In this state they stain badly and irregularly, and have notably lost some of their virulence.

By passing the organism successively through animals, as guinea pigs, rabbits, and mice it acquires an extreme virulence, a subcutaneous injection of a very small quantity sufficing to kill a rabbit or a guinea pig in forty-eight to sixty hours, and a mouse in even a shorter time, sometimes not more than twenty-four hours. Successive cultures upon ordinary media rapidly lose their virulence, but this is easily restored by again passing it through animals.

After death the microbe is found in all the organs and tissues of the body, notably the lymphatic glands, the spleen, liver, and heart blood. The glands near the seat of injection are enlarged and are surrounded by an extensive cedematous effusion, the bubo, which has given its name to the disease. The swelling is not confined to the glands near the seat of injection, but those in other parts of the body are enlarged, sometimes in chains, and all contain the bacillus in nearly pure culture. The spleen contains the microbe in enormous numbers; in animals which have died slowly the organ is enlarged and presents a mottled appearance, studded with white or yellowish minute spots, which spots are aggregations of the microbe in almost pure culture. If the animal has died rapidly the spleen is enlarged to a great size, and is uniformly red in color, the organism being also very abundant. In cases of slow death the organism has been found in the lungs and kidneys, indeed it is always present in the lungs in man in all cases in which there are bronchial or pneumonic symptoms, a by no means rare complication.

The term "almost pure culture" is used advisedly, for the microbe of pest is almost always found associated in animals and man with the pus organisms, notably staphylococci and streptococci, and this is offered as an explanation of the fact that after convalescence from the pest, suppuration of the glands often continues for a considerable time.

If, instead of being inoculated subcutaneously, the animal is subjected to intraperitoneal injection, death is more rapid, the organs are affected in the same way, and the swelling of the superficial lymphatics is replaced by swelling of the mesenteric glands, forming, as it were, internal bubos.

The virulence of the pest bacillus is extreme, and it would seem that a breach of continuity is not necessary for infection, as healthy rats have been caused to contract the disease by being fed either upon a culture of the microbe, or upon the spleen or other organs of an animal dead with the plague.

During the process of growth there is a toxine formed; this is proved by the fact that if a bouillon culture of the microbe is kept for some time at a temperature of 37° C., there are formed, as has before been said, flakes or flocculi, which sink to the bottom of the tube. Now, if these are removed by filtration through a Pasteur-Chamberland filter, there results a slightly turbid liquid in which the absence of micro-organisms can be demonstrated by microscopic examination and cultivation experiments, yet this liquid injected subcutaneously into an

animal will cause its death by an intoxication, and post-mortem examination will demonstrate the absence of the bacillus of pest.

Surpassing in interest, perhaps, the study of the disease itself, is that of the preparation of the serum for the therapeutic and prophylactic treatment of the malady. At this time extensive experiments are being made with it in India, and the results are said to be most favorable, within certain limitations, viz: That the remedy should be administered in sufficient quantities and as early as possible in the course of the disease. Given an ordinary case in the early stages, the hypodermatic injection of 10-25 c. c. of the remedy will usually suffice to produce a rapid amelioration of the symptoms, disappearance of the fever, relief of the profound prostration, and rapid absorption or disappearance of the bubo. In more pronounced or further advanced cases the administration of the remedy must be governed by the course of the disease. A dose of 25 c. c. should be administered at once, and some amelioration of the symptoms will be probably noted; but should these recur, the remedy must be pushed in doses of 10 c. c. or more, until permanent relief is secured or the uselessness of the treatment demonstrated.

I am perfectly aware that in the Indian correspondence of some English medical journals, and in the editorial columns of another the results of the serum treatment of the plague in Bombay have been rather disparagingly spoken of. I pin my faith to the statements of Dr. Roux, who has asserted to me, and in my presence to others, that the reports received by him were satisfactory. Until he sees reason to change his opinion my faith in the remedy will remain unshaken. I am not in possession of statistics, and as they have not been offered me I feel a hesitancy in asking for them. Neither am I prepared to speak from personal observation as to the preparation of the serum, for the reason that I have not as yet arrived at this point in the course which has been marked out for me, and for the additional reason that for obvious reasons the serum is not prepared in Paris, but at a place in the country at some distance. From all I can learn there is no radical departure from the method which has already been outlined by Yersin in the "*Annales de L'Institut Pasteur*." The horse selected for the purpose is treated by intravenous injections of a small quantity of a recent agar culture of pest, suspended in bouillon or sterilized water. The injections are made by the intravenous method, for the reason that in the earlier experiments, when they were made subcutaneously, there was always much swelling and oedema at the site of the injection, and almost invariably the formation of an abscess. After each injection the horse is much prostrated, there are chills, and a fever reaching 40°-41° C. and lasting for several days and gradually subsiding. As the animal is noticeably reduced in flesh and strength by the preparation, it is necessary to exercise great care in increasing and repeating the dose. The process is therefore rather a slow one, nor is a point arrived at where the animal ceases to react to the injection. These reactions are always present, but only become more feeble and last for a shorter period. The treatment is continued and the animal allowed to rest, and a trial made of the strength of the serum. It is the object to have it of such a strength that a dose of one-twentieth to one-tenth of a cubic centimeter will protect a white mouse of about 20 grammes in weight against a lethal dose of the pest culture, not more than forty-eight hours old.

I have had the pleasure of witnessing several series of such experiments in which the animals protected by the serum are still alive and flourishing, while the controls, treated with an equal dose of culture

and protected by a dose of the serum of a normal horse, are long since dead with typical symptoms and post-mortem appearances of pest. The serum of the normal horse was administered to the control animals to avoid any possibility of a claim that there might be a protective influence in any ordinary blood serum.

The serum has certain peculiar properties of its own; added to a turbid emulsion of pest in bouillon in the proportion of one-fiftieth to two-fiftieths, it will in some cases produce an agglutination of the organisms and their subsidence in the liquid, which becomes more or less clear. It is possible that the completeness of this clearing is an index to the potency of the serum, for all serum must be tested by inoculation experiments, and it is not believed that all horses are equally susceptible of immunization.

If the serum is heated to between 50°-60° C. its protective power is much diminished, and at a higher temperature is altogether destroyed; therefore great care must be exercised in the cooling of all pipettes, syringes, and instruments which are used in the inoculations and which have been sterilized by boiling. It is possible that the agglutinating power of the serum mentioned above may form the basis of a clinical test for pest similar to the Widal reaction for typhoid, though, of course, it will be understood that the diagnosis of pest is usually all too easily made.

This, I believe, will about cover all the information on the subject of which I am in possession at the present time, though, of course, something new is developing every day, and further observations will form the basis of subsequent reports. I have also been much interested in witnessing certain experiments made by Dr. Calmette with the serum for the bites of venomous serpents. I have seen rabbits successfully resisting, with the aid of this serum, an intravenous injection of the mixed venom of serpents which caused the death of control animals in from ten to fifteen minutes. It strikes me that the subject might become one of great importance for the people of the United States.

I would feel that I might well be accused of ingratitude if I omitted to make mention here of the uniform kindness and courtesy of which I have been the recipient at the hands of Professor Roux and his assistant, Dr. Borel. Of the former I can only say that language of mine can convey no adequate conception of his enthusiasm as a teacher, the incisiveness and clearness of his speech, and his perfect personal kindness of nature. Instruction under him is a source of perpetual pleasure, and can not help being of the utmost value to the pupil.

I have, sir, the honor to remain, respectfully, yours,

H. D. GEDDINGS,

*Passed Assistant Surgeon, U. S. M. H. S.*

*Smallpox in Memphis, Tenn.*

MEMPHIS, TENN., May 4, 1897.

SIR: I have the honor to report as follows concerning the recent occurrence of smallpox in Memphis:

About the last of March a colored man came to Memphis from Montgomery, Ala., and shortly after his arrival was taken sick. He applied for relief at the city dispensary. The case was diagnosed as smallpox by the physician in charge, and was sent to the county pesthouse. The county health officer, however, did not think it a case of smallpox, in which view he was supported by other physicians, so that I did not report the case. Subsequent events have, however, proved the correct-